

The Place of Radiation Therapy in the Management of Breast Cancer

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MY subject is a very controversial one; indeed, there are few subjects which are accompanied by more controversy than this one. There are those who would entirely exclude radiation therapy as a proper procedure in the management of this disease, and there are others who would make it the method of choice. From both of these views I dissent completely. Actually, the debate is almost entirely as to the extent to which irradiation should augment or even replace surgery in the treatment of this disease, and indecision is expressed even by those of the widest experience. Perhaps one should say that indecision is expressed *particularly* by those of the widest experience.

The entire issue is clouded by three factors: First, prejudice; the unwillingness of too many radiation therapists to concede that their weapon is not all-powerful, and the unwillingness of too many surgeons to concede that surgical treatment does not produce the results that we all devoutly wish it did. Second, the careless and unscientific use of tables of statistics. This is not the place to talk about statistics, but one or two elementary considerations may not be out of place. It is obviously wrong to compare, say, the results obtained in the treatment (by any method) of one hundred Stage IP cases of breast cancer with a like series of clinical Stage I cases treated by another method. It is unscientific to fail to weigh statistical tables for the normal death expectancy and for the normal survival rate. Third, the failure to recognize and to take into consideration the tremendous changes that have occurred in the technic of radiation therapy. The principle of protracted fractional irradiation has completely revolutionized radiation therapy, which bears about the same relationship to the therapy of 20 years ago that modern anesthesia bears to the ether pouring of the eighteen-nineties. Statistical tables based on the older therapy are entirely worthless as a basis of comparison, and practically all of the cases treated more than 15 years ago must be discarded as having no real significance. Thus, Harrington's survey of 3,137 patients followed for five years loses its importance as far as its bearing on the value of radiation therapy is concerned, since 1929 is the latest year in which a patient could have been treated and be included in his survey published in 1935. Greenough, in 1934, published the results of the study of 374 cases of breast cancer treated with external radiation and concluded that

it added little to the patient's chance of survival. But here again the year 1928 is the latest year in which a patient could have been treated and included in this report.

These two authorities are widely quoted as though these figures had some present significance. So far as the place or the value of modern radiation therapy is concerned they are totally devoid of meaning. There are many such surveys in the literature. There is no question as to the ability, sincerity or sound judgment of those who have compiled such studies; it is only that the figures, once valid have lost their significance as to modern irradiation.

"If we are to dispute," said Voltaire, "let us define our terms." I think that there is general agreement that clinical Stage I breast cancer means that the tumor seems to be limited to a lobule of breast tissue; that the skin is uninvolved, and that no axillary or supraclavicular glands are palpable. Pathological Stage I means that no carcinoma cells could be found in the glands removed. Clinical Stage II carcinoma means that the skin is involved, or that palpable glands are present, or both. Pathological Stage II means that the skin was infiltrated, or that metastases to glands were demonstrated, or both. Stage III breast cancer indicates the presence of distant metastases.

A quotation from Pack and Livingston's "Treatment of Cancer and Allied Diseases" will serve as a sort of text for what follows. "Surgery no longer remains unchallenged as the sole method of treatment, or even as the method of choice in the management of any stage or type of mammary carcinoma." From this statement I shall dissent presently, but as a working text it states well the controversial aspect of the problem.

If we accept this dictum, how shall we apply it? What place shall radiation therapy assume? To what extent shall it augment surgery, and when, if ever, shall it be the method of choice?

Radiation therapy may be chosen in place of radical surgery in a Stage I or II tumor: (a) when the patient resolutely refuses surgery, or (b) when for some reason the operative hazard is too great. With but one exception these are the only valid reasons for attacking the disease in Stages I or II by any means other than radical mastectomy. This exception is the inflammatory type of carcinoma. The surgical treatment of this fulminating type of carcinoma is completely hopeless since the line of incision will invariably pass through the dermal and subdermal lymphatics which are plugged with cancer cells. The most radical excision will inevitably be followed by immediate recurrence and death. The

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tumor is extremely radiation sensitive, and good palliative results will follow irradiation. This is an extremely fatal form of breast cancer, and no actual cures or, better, five-year survivals are to be expected. The patient who is treated by irradiation will live longer, however, and in greater comfort, than one subjected to operation.

There is practically unanimous agreement that radiation therapy has no place in the treatment of Stage IP carcinoma, since there is little if any likelihood of improving the excellent results obtained by radical surgery. Since the axilla and supraclavicular regions are, by definition, free from the disease, there seems to be no point to subjecting the patient to the discomfort and expense of irradiation.

STAGE III CANCER

There is little dispute that radiation is the treatment of choice in Stage III breast cancer. Surgery may be useful in the removal of foul ulcerating masses, but in general the patients are given more comfort, and their lives are made more tolerable, by irradiation than by any other method. Interstitial radiation will heal many ulcerating lesions, and there are few things that afford one the satisfaction that results from observation, following irradiation, of the relief from pain due to bone metastases. Superficially ulcerating lesions may be successfully controlled by rather large doses of unfiltered, or very lightly filtered, radiation. If the lesion is not too large, Chaoul or contact therapy offers a simple and easy method of treatment. These methods, with very short anode-surface distances (*e. g.*, 2.0 cm.) and with very large outputs, enable one to give very large amounts of radiation without danger of injury to the deeper structures. With contact therapy, for example, the dose at a depth of 1.0 cm. is only 30 per cent of the surface dose, while at a depth of 4.0 cm. it is practically negligible. With larger ulcers, more than 3.0 cm. in diameter, low voltage unfiltered radiation may be employed. Platinum needles containing radium element may be introduced and left in place for periods of from 120 to 140 hours.

The following is an illustrative case: A 64-year-old woman was seen in September, 1939, with a history of a mass in the lower lateral quadrant of the left breast for three years past. As she had arthritis in her fingers, she had hoped that the breast tumor was part of the same process and, hence, had sought no advice. The mass had been painful for ten months preceding her first visit. She had a mitral heart lesion which was rather poorly compensated and required digitalis. Examination showed a hard mass, 6 x 5 x 3 cm., adherent to the skin of the breast, and with a soft area underlying a reddish purple skin, obviously about to ulcerate. There were massive rock-like axillary glands which were entirely immovable. Under novocain infiltration anesthesia, 15 platinum needles, having a wall thickness of 0.5 mm. pt. and each containing 1.0 mg. radium, were imbedded in the mass for 130 hours. High voltage x-ray therapy was directed at the axillary masses. Two months later the breast tumor was barely palpable, the axillary

glands were reduced about 50 per cent, and all pain had disappeared. The patient had no recurrence of the breast tumor, nor did the axillary glands increase in size. She lived four years and died in congestive heart failure at the age of 68 years.

As to clinical Stage I cancer, I repeat that radical surgery is the method of choice. Occasionally, however, a patient will refuse to submit to operation, and there remains no choice but to employ irradiation. That this is not always unsuccessful is illustrated by the following cases: A woman aged 46, had a small mass in the upper and outer quadrant of the right breast, and submitted to biopsy. The pathological diagnosis was adenocarcinoma, Grade III. She firmly refused mastectomy and was treated only with external radiation therapy. The mass disappeared promptly and the patient is free from any evidence of disease six and one-half years later. I cite this case only as an interesting example of what may sometimes be accomplished and not to indicate that x-ray therapy should ever be the method of choice.

STAGE II CANCER

With this rather summary dismissal of the problems of Stage I and Stage III breast cancer, we find ourselves at the crux of the controversy, namely, how shall we treat Stage II cancer? How shall irradiation augment mastectomy; shall it be given before or after surgery, or both times, and when shall it replace surgery as the method of choice?

There is, in my belief, no justification for ever using irradiation rather than surgery. Stage II cancer of the breast, except inflammatory carcinoma, is best attacked by radical mastectomy and I would be unwilling to allow any exception to this unless it be the two previously noted, *i. e.*, the patient refuses surgery, or the surgeon is unwilling to operate because of certain hazards.

There is rather general agreement that postoperative irradiation is imperative in the more anaplastic tumors of Grades III and IV. In the case of the more differentiated Grades I and II, agreement is not so unanimous. For myself, I am unwilling to accord so much prognostic value to tumor grading, for two reasons: (1) Unless multiple sections are made of practically the entire tumor no one can be sure that the growth reported as Grade II may not exhibit, five millimeters away, the lack of differentiation characteristic of Grade IV. (2) Radiation sensitivity is a purely relative thing. That a given tumor is highly radiation sensitive does not mean that it is radiation curable, nor does radiation resistant mean that no cellular effects can be produced. These terms mean only that some cells are more easily influenced than others, but a moment's reflection will persuade anyone that all cells may be influenced or even destroyed by irradiation.

It is not unreasonable, then, to maintain that all Stage II breast cancers should be irradiated. If the objection is made that statistics show a not very impressive increase in the five-year survival rate, there are two replies possible to the objection. If the increase were only 5 per cent, and if the five hap-

pened to include the objector's mother, wife or sister, the objection would become less valid. As it is, the survival rate is pretty bad; even a very little increase is desirable.

Moreover, here again the statistical tables must be viewed rather skeptically. Very few of them included any large series of patients irradiated with modern technique, and until we have accumulated such series the validity of these tables, in so far as the value of postoperative irradiation is concerned, is very doubtful. There is even greater dispute as to the desirability of preoperative radiation therapy. As a matter of fact, we do not know much about it. If there are any large series of cases treated by preoperative irradiation and radical mastectomy and followed for five years, I am unaware of them. Adair has reported a series and failed to find any appreciable improvement in the five-year results, but he neglected to point out that the patients included in his series were treated with a single dose of 700 r. To argue that such a series has any significance is like maintaining that amputation of the leg is a formidable procedure carrying a very high mortality rate, and supporting the claim by a reference to the mortality tables of the Civil War.

There are definite objections to preoperative irradiation. There is no way to know, for example, whether we are dealing with Stage I or Stage II cancer. One is likely to be encouraged to treat cases without a histological diagnosis having been made. Subsequent operation is unquestionably made more difficult, and the plastic results are likely to be less pleasing. A certain amount of time is lost in awaiting the completion of the irradiation and the subsidence of the subsequent reaction. On the other hand, one cannot but be impressed with the number of breasts removed and found sterile which had previously contained cancer.

The pros and cons of the question are thus somewhat balanced, and until someone has accumulated a significant number of cases thus treated, we had best suspend judgment.

There remains one question which should be answered: "Of what value, if any, in the treatment of breast cancer, is castration?" Here again, there is no sufficient weight of evidence to warrant a dogmatic statement. Cancer of the breast seems to be more lethal in menstruating women than in those past the menopause. The periodic engorgement of the breasts at or before menstruation is a familiar phenomenon, making it clear that the estrogenic substances secreted by the functioning ovary have a

profound influence on breast tissue. It is known that breast cancer can be produced in mice by the injection of large doses of estrogenic substances. When one weighs these considerations against the harm that may possibly follow depriving a woman of her ovarian function, remembering that her life is at stake, it seems reasonable to add to our armamentarium the method of castration at least until it is proven to have no value. Irradiation of the ovaries of the postmenopausal woman is quite useless.

CONCLUSIONS

1. Irradiation therapy must not be evaluated on the basis of statistical surveys as much as ten years old.
2. Stage I mammary carcinoma should not be irradiated, but should be treated by radical mastectomy.
3. Stage III carcinoma of the breast should but rarely have any surgery, but should be treated entirely with irradiation.
4. Stage II breast cancer should be treated by radical mastectomy plus postoperative irradiation. The value of preoperative therapy is not established, but may be great.
5. There is little to lose and perhaps much to gain by the castration of menstruating women who have breast cancer.

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QUESTIONS AND ANSWERS

DR. GOIN: First question: "In Stage I cancer of the lower and inner quadrant where metastases may be inward and unrecognized would you use radiation therapy?"

No, I would not. The patient either does or does not have metastases. If she does, she will not be cured anyway, and if she does not she will likely be cured by the mastectomy. In general these cases must be dealt with as they present themselves.

Next question: "Do you feel it logical to treat the breast area postoperatively after adequate radical mastectomy—assuming you are going to treat the axilla and superclavicular area?"

Yes, I think that it is, because skin recurrences in the operative field are quite common.

Next question: "Please repeat the treatment of Stage III cancer of the breast relative to x-ray."

I said—and if I didn't I should have said—that it is entirely a matter of making the patient's life tolerable. We are not going to cure Stage III breast cancer. Radiation therapy will make life much more tolerable. Small surface ulcerations can well be treated by large doses of superficial x-ray therapy. Larger ones may be treated by intramural implantation of needles containing radium element. In general the results are fairly gratifying.